Endoscopy showed resolution of GvHD in the colon and duodenum. Video visualization was performed to evaluate the distal small bowel using the M2A endoscopic capsule by Given Imaging. The duodenum and colonic mucosa appeared normal, but the jejunum and ileum had severe diffuse bleeding ulcerations. The video capsule is 11mm × 26mm, weighs less than 4 grams, has a field of view of 140 degrees, and can detect lesions less than 0.1mm. The camera takes pictures for 8 hours and generates approximately 57,000 images at 2 frames per second. Contraindications include suspected obstruction or stricture, presence of a cardiac pacemaker, or a swallowing disorder. Video visualization gives valuable information on the status of the distal small bowel that cannot be obtained by fiberoptic endoscopy and may aid in evaluation of GvHD following allogeneic BMT.

244

SOLUBLE TUMOR NECROSIS FACTOR RECEPTOR: ENBREL (ETANERCEPT) FOR THE TREATMENT OF IDIOPATHIC PNEUMONIA SYNDROME FOLLOWING ALLOGENEIC STEM CELL TRANSPLANTATION

Yanik, G.A.[1], Uberti, J.P.[1], Ferrara, J.L.M.[1], Levine, J.E.[1], Hutchinson, R.J.[1], Ho, V.T.[2], Cooke, K.R.[1] 1. University of Michigan Medical Center, Ann Arbor, MI; 2. Dana-Farber Cancer Institute, Boston, MA

Non-infectious lung injury is as a frequent and severe complication of allogeneic bone marrow transplantation (BMT). In the acute setting, a diffuse non-infectious process termed Idiopathic Pneumonia Syndrome (IPS) may occur. Despite advances in supportive care and the use of high dose steroids, mortality from IPS remains unacceptably high (> 70%). Etanercept is a soluble tumor necrosis factor (TNF) receptor, consisting of two soluble p75 TNF receptors fused to the Fc portion of a human IgG1. A trial examining etanercept in the treatment of IPS following allogeneic transplant has now been undertaken. Fourteen patients (median 18 yrs, range 1-60 yrs), each meeting the diagnostic criteria for IPS were treated. Broncho-alveolar lavage (BAL) specimen were obtained pre and post therapy, undergoing analysis for both infectious pathogens (viral, bacterial, fungal, PCP, AFB) and for inflammatory cytokine markers (TNF, TNFR1, sCD-14, LBP, and MCP-1). Patients in whom the pre-therapy BAL was positive for a potential pathogen (by specific stain or culture) were ineligible for therapy. Etanercept was administered subcutaneously at a dose of 0.4 mg/kg (maximum dose 25 mg) twice weekly, for a maximum of 8 doses. All patients required supplemental oxygen at therapy onset, with seven patients requiring mechanical ventilation. Etanercept therapy was initiated a median of 17 days (range 11-87 days) post transplant. **Results:** Therapy was well tolerated, with no infusion related reactions. Eight of 14 patients had a complete response, defined as the ability to withdraw completely from supplemental oxygen support. In those responding, the median time to complete response was 7 days (range 3-18 days), and the median time to normalization of radiographic findings was 6 days (range 2-10 days). Two other patients had a significant reduction in their FiO2 requirement during therapy. Three patients died while on therapy, from progressive organ dysfunction. Post therapy BAL fluid analysis noted a significant reductions in all inflammatory cytokines tested, including TNFa, TNFR1, sCD14, LBP and MCP-1 (Table below). **Conclusion:** Etanercept therapy was well tolerated, with minimal toxicity and favorable response in patients with IPS post allogeneic transplant. The clinical and biochemical responses seen with therapy support a mechanistic role for TNFa in the pathogenesis of this disorder. Further trials, investigating the responsiveness of IPS to etanercept therapy are warranted.

Table. *BAL Fluid: Mean Values Pre- and Post-Etanercept Therapy*

	n	TNF (pg/mL)	TNFR1 (ng/mL)	sCD-14 (ng/mL)	LBP (ng/mL)	MCP-1 (ng/mL)
Control-A	3	5.2 (0-16)	.02 (.02-.03)	0 (0)	0 (0)	0.04 (.015-0.07)
Control-B	10	5.4 (0-23)	.11 (.02-.37)	1.9 (0-8.8)	0 (0)	0.28 (0.02-1.0)
IPS pre-Tx	7	93 (0-500)	.86 (.08-1.5)*	82.6 (0-250)*	331 (0-1000)*	20 (0.6-73.9)
IPS post-Tx	5	16 (10-23)	.18 (.1-0.36)†	3.0 (0-6.2)	0 (0)	0.07 (.05-0.1)†

Controls were (A) a group of healthy volunteers or (B) transplant patients without IPS. *$P < .05$, IPS pre-tx versus Control-B, †$P < .05$, IPS post-tx versus IPS pre-therapy.

245

NEUROLEPTIC MALIGNANT SYNDROME FOLLOWING STEM CELL TRANSPLANTATION

Craig, M., Ericson, S., Schunn, G., Beall, C.L. Mary Babb Randolph Cancer Center, West Virginia University, Morgantown, WV

Neuroleptic malignant syndrome (NMS) is a rare disorder presenting with hyperthermia, muscle rigidity, autonomic instability, and altered consciousness. Although NMS is usually associated with antipsychotic medications, it has also been described in patients receiving antiemetics. The estimated incidence in susceptible populations is about 0.2%, with an associated mortality rate 10-20%. Three cases of NMS following bone marrow or peripheral blood stem call transplantation have been described in the medical literature. We present an additional patient for review. A 51 year-old female underwent autologous peripheral blood stem cell transplantation for IgA kappa multiple myeloma with high dose melphalan. She achieved engraftment on day +14. Her post-transplantation course was complicated by persistent nausea and vomiting requiring treatment with prochlorperazine or promethazine. On day +20, she developed fever of 39.4°C, labile blood pressure, elevated pulse, and delirium. Antimicrobials were begun for presumed sepsis. Cultures were negative. By day +21, her temperature had climbed to 40.9°C, delirium continued, and muscle rigidity developed, with an elevation in CK. She had a generalized tonic-clonic seizure. NMS was diagnosed based on her clinical scenario and all antiemetics were discontinued. Dantrolene sodium was initiated IV. Response occurred with resolution of temperature, decreased muscle rigidity, and improved mental status within 24 hours. Previous reports of NMS following transplantation include 2 cases diagnosed 9 and 11 days following autologous transplantation for liposarcoma and breast cancer (Garrido SM, et al. Bone Marrow Transplantation 1998;21:427-8). Another was seen 6 days after allogeneic transplant for AML (Onose M, et al. Bone Marrow Transplantation 2002;29:803-4). Two had received haloperidol, while another received prochlorperazine and droperidol. All three responded to discontinuing offending medications and supportive care. There were no deaths. The recognition of NMS in the post-transplantation setting is confounded by multiple etiologies for fever and delirium in these patients. The pathology of the disorder is felt to relate to dopamine blockade. Initial treatments involve stopping inciting medications and supportive care. Pharmacological interventions such as bromocriptine, dantrolene sodium, and benzodiazepines should be used to shorten duration of symptoms and improve survival.

246

TACROLIMUS CONVERSION FROM INTRAVENOUS (I.V.) TO ORAL (P.O.) IN ALLOGENEIC STEM CELL TRANSPLANTATION

Zimmerman, R.L., Petersen, K.A., Hardiman, P.S., Davis, T.L., Lynch, J.C., Devetten, M.P. University of Nebraska Medical Center, Omaha, NE

Tacrolimus (FK506) is commonly used in allogeneic stem cell transplantation (SCT) to prevent rejection and graft-versus-host disease. Dosing recommendations are mostly based on studies performed in solid-organ transplant recipients. The package insert recommends a conversion rate of 1:4 when changing from the intravenous to the oral formulation. We retrospectively reviewed tacrolimus levels and toxicity in 32 patients who underwent allogeneic SCT between July 2001 and June 2003 using the package insert recommended conversion rate. All patients started tacrolimus on day -1 at a dose of 0.03 mg/kg actual body weight by continuous IV infusion. Levels were drawn peripherally on day +1, +3, +5 and then biweekly. Target range for tacrolimus levels was 8-12 ng/mL. Conversion from IV to PO at a conversion rate of 1:4 occurred when patients could tolerate P.O. medication. Thirty-two patients underwent alloSCT for a variety of hematologic malignancies. Median age at the time of transplant was 43 year (range 19-58), 78% underwent a MRD donor SCT, 3% a 5/6 MRD SCT, and 19% a MUD SCT, conditioning was Cy/TBI (89%) or Bu/Cy2 (11%). Ninety-three percent of patients with available data required at least one IV dose reduction, the median day of IV to PO conversion was +11 (range +7-+25). The median